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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,841	06/26/2003	Rashid A. Fawwaz	0575/66697/JPW/AJM/DNS	7635

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
07/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/608,841	FAWWAZ, RASHID A.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 7-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 7-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Second Notice to Comply*.

DETAILED ACTION

Applicant's amendment and response received on 4/23/07 has been entered. Claims 5-6, and 22-26 have been canceled. Claims 1-4 and 7-21 are currently pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Specification

The objection to the disclosure because of informalities, including reference in the specification on page 10 line 18 to a "Table I" not present in the as filed specification, is withdrawn in view of the amendments to the specification.

Nucleotide and/or Amino Acid Sequences

Applicant's submission of a sequence listing in both paper format and CRF and the accompanying statement that the contents of both are the same is acknowledged. Further, applicant's amendment of the specification on page 12 to insert a SEQ ID NO after the recitation of an amino acid sequence has been entered. However, the submitted CRF does not match the application specification. Thus, this application continues to fail to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Second Notice To

Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Appropriate correction is required.

Please note that the time period for response to the Notice to Comply is the same as that for the instant office action. A response to this office action must include a response to the Notice to Comply to be considered complete.

Claim Rejections - 35 USC § 102

The rejection of claims 22-23, and 25 under 35 U.S.C. 102(b) as being anticipated by Fawwaz et al. (1997) Proc. Am. Assoc. Cancer Res., Vol. 38, page 612, abstract #4110 (IDS of 2/3/05), is withdrawn in view of cancellation of these claims.

The rejection of claims 22-26 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,861,156 (1/19/99), hereafter referred to as George et al., is withdrawn in view of applicant's cancellation of these claims.

The rejection of claims 1, 22-23, and 25 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,328,985 (7/12/94), hereafter referred to as Sano et al., is withdrawn over canceled claims 22-23 and 25, and over pending claim 1 in view of the amendments to the claim which now recite that the streptavidin is administered to a subject after an allogenic transplant in an amount effective to inhibit immunological rejection.

Claim Rejections - 35 USC § 112

The rejection of previously pending claims 1-26 under 35 U.S.C. 112, first paragraph, for scope of enablement is withdrawn over canceled claims 5-6 and 22-26, and maintained over amended claims 1-4, and 7-21. Applicant's claim amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The previous office action identified the following scope of enablement: the specification, while being enabling for methods of delaying the rejection of an allograft in a subject comprising transplanting an allogeneic tissue or organ to a subject and administering by intraperitoneal injection 20 mg/kg of streptavidin for five consecutive days starting on the day of transplant, does not reasonably provide enablement for inhibiting the rejection of any transplant, and in particular a xenogenic transplant, comprising administering at any time before or after transplantation of an organ, tissue, or cells, an amount of streptavidin using any route of administration, including intravenous or subcutaneous. Applicant's amendments to claim 1 have overcome the grounds of rejection pertaining to inhibition of rejection of a xenotransplant, and further the grounds of rejection pertaining to administration of streptavidin before transplantation. However, the remaining grounds of rejection concerning routes of administration and dosage regimen of streptavidin are maintained.

The applicant argues that claim 1 has been amended to recite that the streptavidin is administered "at a suitable time after transplant" and in an amount "effective to inhibit immunological rejection of the transplant", and that since the examiner has found that intraperitoneal administration of 20 mg/kg of streptavidin on days 1-5 post transplant is enabled

that based on the teachings of the specification and knowledge of the skilled artisan that it would not require undue experimentation to determine other effective routes of administration and dosage regimens. This is not agreed as the previous office action provided a detailed analysis of why the such experimentation would in fact be undue as a result of the state of the art for using streptavidin at the time of filing and the unpredictability at the time of filing for affecting the activity of any immune cell by the administration of streptavidin. This analysis is reiterated below for applicant's convenience.

The previous office action stated that the specification teaches on page 2 that there is no known nexus between streptavidin and the inhibition of immunological rejection, and later states on page 12 that the underlying mechanisms of graft prolongation by streptavidin has not yet been determined. At the time of filing, streptavidin was commonly used as a binding partner for biotin in a variety of applications ranging from in vitro assays to in vivo diagnostics and therapy. The applicant previously published work demonstrated that intraperitoneal administration of streptavidin was capable of a statistically significant antiproliferative effect on a human breast cancer xenograft in nude mice. However, none of the prior art references of record demonstrate that streptavidin is capable of having any type of effect on any immune effector cell, including T cells, or B cells *in vitro* or *in vivo*. In fact, the prior art contains numerous teachings for the use of streptavidin in various immunoconjugates for the purpose of stimulating an immune response through targeting of immune effector cells to various cells of interest. See for instance U.S. Patents 5,861,156 and 5,328,985 cited above. Thus, the applicant's working examples provide a single example of conditions under which streptavidin is apparently capable of delaying allograft rejection. These conditions include the intraperitoneal injection of the streptavidin and a dosage

regimen of 20 mg/kg for 5 days starting on the day of transplant. While the specification contemplates other embodiments, including intravenous or subcutaneous administration, and the administration of a single dose of streptavidin from 2 mg/kg to 200 mg/kg, the applicant's working examples provides no demonstration that any conditions other than those actually tested can achieve any effect on allograft rejection.

Further, the claims as amended still broadly recite that the streptavidin is administered "at a suitable time after transplant" to inhibit immunological rejection. The specification on page 5 defines a "suitable time" as "any time at which streptavidin administered would be expected to inhibit the immunological rejection of the transplant". The definition goes on to give some preferred examples, including one to five days after transplant, but stresses that a "suitable time" is not limited to these particular times. However, aside from the administration of streptavidin from days one to five post transplant, the specification fails to provide any specific guidance that single or multiple administrations of streptavidin at any other time points can have any effect on graft rejection. It is particularly noted that the rejection of third party allografts transplanted 60 days after a 5 day course of streptavidin did not differ from untreated controls. Thus, the specification fails to provide sufficient guidance as to any "suitable time" for streptavidin administration other than administration on days 1-5 post transplant.

Therefore, given the extensive body of literature concerning the activity and use of streptavidin both *in vitro* and *in vivo*, including the use of streptavidin in methods of immunostimulation, the state of the art of allograft and xenograft transplantation as taught by Kaufman, the single example of conditions under which streptavidin is capable of affecting allograft rejection, and the breadth of the claims, it would have required undue experimentation

to test all the various parameters involved in the instant methods to find alternative conditions under which streptavidin would inhibit graft rejection. Thus, the specification is only enabling for methods of delaying the rejection of an allograft in a subject comprising transplanting an allogeneic tissue or organ to a subject and administering by intraperitoneal injection 20 mg/kg of streptavidin for five consecutive days starting on the day of transplant

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all

official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633

Application No.: 10/608,841

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☒ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: the CRF does not match the application specification

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☐ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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